AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting an organism having altered activity or expression of a cholinergic pathway molecule selected from the group consisting of EGL-8, RIC-8 and RIC-4 or mammalian orthologue thereof, and altered activity or expression of ~~an insulin signaling pathway molecule~~ DAF-2 or mammalian orthologue thereof with a test agent, wherein said altered activity or expression of the cholinergic pathway molecule or said altered activity or expression ~~of the insulin signaling pathway molecule~~ said DAF-2 or mammalian orthologue thereof extends the mature life phase of the organism;

assaying for the ability of the test agent to increase the lifespan of the organism as compared to a suitable control, and

selecting an agent that increases the lifespan,

to thereby identify an agent capable of extending the mature life phase of an organism.

Claims 2-13

14. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting an organism with a test agent, said organism having a cholinergic pathway;

assaying for the ability of the test agent to inhibit the ~~cholinergic pathway by monitoring the effect of the test agent on~~ one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the indicator of said cholinergic pathway is selected from the group consisting of ~~muscarinic receptor, EGL-30,~~ EGL-8, RIC-8~~, DAG~~ and RIC-4, ~~UNC-13,~~ or a mammalian orthologue thereof; and

selecting an agent that inhibits the cholinergic pathway;

to thereby identify an agent capable of extending the mature life phase of an organism.

15. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting an organism with a test agent, said organism having a cholinergic pathway and an insulin signaling pathway;

assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by:

(i) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of at least one indicator of said cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting of ~~muscarinic receptor, EGL-30,~~ EGL-8, RIC-8~~, DAG~~ and RIC-4, ~~UNC-13,~~ or a mammalian orthologue thereof; and

(ii) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization~~, or synaptic release of at least one indicator of said insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof;

and selecting an agent that inhibits the cholinergic pathway and ~~insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof;

to thereby identify an agent capable of extending the mature life phase of an organism.

16. **(Cancelled)**

17. **(Currently Amended)** The method of claim ~~16~~ 14, wherein the agent is identified based on its ability to alter expression of said indicator.

18. **(Currently Amended)** The method of claim ~~16~~ 14, wherein the agent is identified based on its ability to alter an intracellular ~~or extracellular~~ level of said indicator.

19. **(Currently Amended)** The method of claim ~~16~~ 14, wherein the agent is identified based on its ability to alter an activity of said indicator.

20. **(Currently Amended)** The method of claim ~~16~~ 14, wherein the agent is identified based on its ability to alter the cellular localization of said indicator.

21. **(Original)** The method of any one of claims 1, 2, 14 and 15, wherein the organism is a nematode.

22. **(Original)** The method of claim 21, wherein the nematode is *C. elegans.*

23. **(Original)** The method of claim 21, wherein the nematode is a parasitic nematode.

24. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting a cell with a test agent, said cell having a cholinergic pathway;

assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting of ~~muscarinic receptor, EGL-30,~~ EGL-8, RIC-8~~, DAG~~ and RIC-4, ~~UNC-13,~~ or a mammalian orthologue thereof; and

selecting an agent that inhibits the cholinergic pathway;

to thereby identify an agent capable of extending the mature life phase of an organism.

25. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting a cell with a test agent, said cell having a cholinergic pathway and an insulin signaling pathway;

assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by:

(i) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway, wherein the indicator of said cholinergic

pathway is selected from the group consisting ~~muscarinic receptor, EGL-30,~~ EGL-8, RIC-8~~,~~ ~~DAG~~ and RIC-4, ~~UNC-13~~, or a mammalian orthologue thereof;

(ii) and monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, ~~, or synaptic release of at least one indicator of said insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof; and

selecting an agent that inhibits the cholinergic pathway and ~~insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof;

to thereby identify an agent capable of extending the mature life phase of an organism.

26. **(Currently Amended)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting a cell population with a test agent, said population comprising a cell having a cholinergic pathway and a cell having an insulin signaling pathway;

assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by:

(i) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting ~~muscarinic receptor, EGL-30,~~ EGL-8, RIC-8~~,~~ ~~DAG~~ and RIC-4, ~~UNC-13~~, or a mammalian orthologue thereof;

(ii) and monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, ~~, or synaptic release of at least one indicator of said insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof; and

selecting an agent that inhibits the cholinergic pathway and ~~insulin signaling pathway~~ DAF-2 or a mammalian orthologue thereof;

to thereby identify an agent capable of extending the mature life phase of an organism.

27-33. (**Canceled**)

34. **(Currently Amended)** The method of any one of claims 24-26, wherein the agent is identified based on its ability to alter expression of said indicator of said cholinergic pathway.

35. **(Currently Amended)** The method of any one of claims 24-26, wherein the agent is identified based on its ability to alter an intracellular or extracellular level of said indicator of said cholinergic pathway.

36. **(Currently Amended)** The method of any one of claims 24-26, wherein the agent is identified based on its ability to alter an activity of said indicator of said cholinergic pathway.

37. **(Currently Amended)** The method of any one of claims 24-26, wherein the agent is identified based on its ability to alter the cellular localization of said indicator of said cholinergic pathway.

38. **(Original)** The method of any one of claims 24-26, wherein the cells are mammalian cells.

39. **(Original)** The method of any one of claims 24-26, wherein the cells are human cells.

40. **(Original)** The method of any one of claims 24-26, wherein the cells are derived from a nematode.

41. **(Original)** The method of claim 26, wherein the cell population comprises presynaptic cells and postsynaptic cells.

42. **(Original)** The method of claim 41, wherein the presynaptic cells are nerve cells.

43. **(Original)** The method of claim 41, wherein the postsynaptic cells are nerve cells.

44. **(Original)** The method of claim 41, wherein the postsynaptic cells are muscle cells.

45-56 **(Cancelled)**

57. **(New)** A method for identifying an agent capable of extending the mature life phase of an organism, comprising:

contacting an organism with a test agent, said organism having a cholinergic pathway and decreased activity or expression DAF-2 or mammalian orthologue thereof;

assaying for the ability of the test agent to inhibit the expression or activity of an indicator of said cholinergic pathway selected from the group consisting of EGL-8, RIC-8 and RIC-4, or a mammalian orthologue thereof;

wherein the ability of said agent to inhibit the expression or activity of said indicator of said cholinergic pathway identifies said agent as capable of extending the mature life phase of an organism.